Optimal Medical or Mechanical Treatment for Patients with Aborted Sudden Cardiac Death due to Coronary Spasm

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Life-threatening ventricular arrhythmias and pulseless electrical activity due to coronary artery spasm may lead to aborted sudden cardiac death (ASCD). Implantable cardioverter-defibrillator (ICD) had been implanted in majority of these patients. In the previous reports, just a quarter of these patients had appropriate ICD shocks during the follow-up periods of 41 ± 28 months. Although sufficient medications including multiple vasodilators were the first line therapy, less medication were frequently observed in patients with ASCD due to coronary artery spasm in the clinic. One-quarter patients with ASCD due to coronary artery spasm after the implantation of ICD had appropriate ICD shocks under the medications during the follow-up periods, whereas the remaining three-quarter patients had no appropriate ICD shocks. If cardiologists performed the sequential spasm provocation tests under the sufficient medications in ASCD patients due to pure coronary spasm as one of option for the ICD implantation, we may classify these ASCD patients for the requirement of ICD implantation to suppress the next life-threatening ventricular arrhythmias in the future.

KEY WORDS: aborted sudden cardiac death, implantable cardioverter-defibrillator, pacemaker, pulseless electrical activity, vasospastic angina, ventricular fibrillation

I. Introduction

Life-threatening ventricular arrhythmias after resuscitated from aborted sudden cardiac death (ASCD) in patients with pure vasospastic angina (VSA) are a serious major problem in the clinic. Under the sufficient medical therapy including multiple vasodilators, the majority of VSA has a favorable clinical outcome, whereas patients with ASCD due to pure coronary artery spasm may have an adverse prognosis. Implantable cardioverter-defibrillator (ICD) was effective in patients with structural heart disease and ventricular fibrillation/tachycardia. The majority of clinical reports concluded that the implantation of ICD was effective to suppress the next fatal events in patients with ASCD due to coronary artery spasm. However, just one-quarter patients with ASCD due to coronary artery spasm after the implantation of ICD had appropriate ICD shocks during the follow-up periods. Manero et al reported that the frequency of appropriate ICD shocks was 24.5% (12/49) in patients with ASCD due to coronary artery spasm. We had no precise definition of which ASCD patients due to coronary spasm should be necessary to implant the ICD to suppress the next fatal serious arrhythmic events. In this review, I mentioned the optimal medications and mechanical therapy in patients with ASCD due to pure coronary spasm and I also described the necessity of spasm provocation testing under the sufficient medications as well as the implantation of ICD.

II. Vasodilators in patients with ASCD due to coronary spasm

As shown in Table 1, 313 (94%) out of 333 patients with ASCD due to coronary spasm had calcium-channel blockers (CCBs), while nitrate was administered in 241 patients (72.4%). We could not find the number of CCB in paper by Ahn et al. In 145 patients with ASCD due to coronary spasm, 116 patients (80%) had just one CCB, whereas multiple CCBs were administered in 20 patients (13.8%) including 19 patients (13.1%) with two CCBs and 1 patients (0.7%) with three CCBs. Nine patients (6.2%) had no CCB. As shown in Table 2, one vasodilator was observed in 44 patients (30.3%), while two vasodilators were found in 70 patients (48.3%). More than three vasodilators were recognized in 27 patients including 23 patients (15.9%) with three vasodilators and 4 patients (2.8%) with four vasodilators, whereas 4 patients had no vasodilators. Mean vasodilator number was 2.6 ± 0.9 by Ahn et al, 1.5 ± 0.7 by Manero et al, or 2.0 ± 0.8 by Sueda et al. In Korean patients with vasospastic angina (VSA) without ASCD, mean vasodilator number was 2.3 ± 0.8. Table 3 showed that the mean vasodilator number in patients...
The mean number of vasodilators was significantly lower in patients with appropriate ICD shocks (1.58 ± 0.87 vs. 1.94 ± 0.81, p<0.05).

### III. Less medication in patients with ASCD due to coronary spasm after the implantation of ICD

We could analyze the medications in 139 out of 180 patients with ASCD due to coronary spasm and after the implantation of ICD\(^{11}\). One CCB was administered in 110 patients (79.1%), while the remaining 19 patients (13.7%) had taken two CCBs and another one (0.7%) had three CCBs. As a result, just 14.4 percent of these 139 patients had taken two or more CCBs. One vasodilator was administered in 41 patients (29.5%), whereas two, three, four vasodilators were administered in 66 patients (47.5%), 23 patients (16.5%), and 4 patients (2.9%), respectively. Only 27 patients (19.4%) had taken more than three vasodilators. In the real world, we could find the powerful medications...
including over two CCBs or over three vasodilators in the minority of patients with ASCD due to coronary spasm after the implantation of ICD. Cardiologists should reconsider the medications after the implantation of ICD due to coronary spasm. It may be better to administer the two or more CCBs with different working mechanism such as dihydropyridine or benzodiazepine.

IV. Ventricular fibrillation or tachycardia

Serious fatal arrhythmias such as ventricular fibrillation or tachycardia sometimes occurred in patients with severe VSA. ICD was implanted in the majority of these ASCD patients due to coronary spasm. However, according to the Japanese Circulation Society (JCS) guidelines for diagnosis and treatment of coronary spastic angina, ICD implantation is defined as one option. Furthermore, according to the JCS/Japan Heart Rhythm Society guidelines on non-pharmacotherapy of cardiac arrhythmia, ICD implantation was defined as class IIa when patients were at high risk of next life-threatening ventricular arrhythmias due to refractory coronary artery spasm. If patients had no resistant coronary spasm, ICD implantation was defined as class IIb. ICD implantation may not be always necessary in patients with life-threatening ventricular arrhythmias due to pure coronary artery spasm under the sufficient medications. As shown in Fig. 1, when abnormal coronary vasoconstriction is recognized after the sequential spasm provocation tests under abundant medications, cardiologists may prefer to select the implantation of ICD. However, cardiologists may be able to select to free discussion for ICD implantation if the sequential spasm provocation tests under sufficient medications document no abnormal coronary responses.

V. Unknown cause of ASCD

Some ASCD patients due to coronary spasm had unknown causes. These patients with ASCD may have the opportunity of ventricular fibrillation or tachycardia, pulseless electrical activity, complete atroventricular block or their combined states in the clinic. When no pathological vasoconstriction is observed after the sequential spasm provocation test, ICD implantation may be one of choice after the individual discussion. In contrast, ICD implantation may be necessary for ASCD patients due to unknown cause who had abnormal pathological vasoconstriction under the sequential spasm provocation tests as shown in Fig. 1.

VI. Pulseless electrical activity (PEA)

We reported a case with PEA due to severe coronary spasm without occurrence of ventricular fibrillation or tachycardia. He was successfully resuscitated without any irreversible complications under the cardiopulmonary support for more than a quarter hour. In the previous reports, one patient with coronary spasm died due to electromechanical dissociation and severely reduced left ventricular contraction despite of the appropriate ICD therapy for ventricular fibrillation. Another patient presented to the hospital with ASCD after chest pain, and electrocardiography at the emergency department showed PEA. An intra-cardiac electrocardiogram showed no ventricular arrhythmia,
and this patient was successfully resuscitated\(^6\). If PEA occurred in patients with ASCD due to coronary artery spasm after the implantation of ICD, ICD may not be effective to improve the serious fatal events except the occurrence of ventricular fibrillation after the PEA. ICD implantation is controversial in patients with PEA due to coronary artery spasm. Just manual cardiopulmonary support may be effective for the above PEA patients to recover the irreversible events. As shown in Fig. 2, ICD implantation may be one of choice when the sequential spasm provocation tests documents provoked spasm. In contrast, ICD implantation may be individual discussion if no provoked spasm was observed after the sequential spasm provocation tests under the abundant medications.

VII. Complete atrioventricular block

We sometimes experience ASCD patients with complete atrioventricular block due to pure coronary artery spasm. It may be related to the ischemia on the atrioventricular artery. The electrical stimulation of right ventricle is necessary for these events as well as the administration of vasodilators. In the previous reports, cardiologists might implant a pacemaker in these patients, while cardiologists now may select to implant an ICD. Cardiologists should select to implant the intravenous ICD but not subcutaneous ICD because of short limiting time for pacemaker function in subcutaneous ICD. However, pacemaker or ICD implantation is controversial in ASCD patients with complete atrioventricular block due to coronary artery spasm. As shown in Fig. 2, ICD implantation may be individual discussion if no provoked spasm was observed after the sequential spasm provocation tests under the sufficient medications. However, intravenous ICD implantation may be one of choice when the sequential spasm provocation tests documents provoked spasm.

VIII. Effect of ICD implantation in patients with ASCD due to coronary artery spasm

In 180 patients with ICD implantation after ASCD due to coronary artery spasm, appropriate ICD shocks were recognized in 44 patients (24.4\%) during the follow-up periods\(^{11}\). Appropriate ICD shocks were effective to suppress the ventricular tachycardia in 3 patients, ventricular tachycardia or fibrillation in 9 patients and ventricular fibrillations in 32 patients. Irrespective of the implantation of ICD in patients with ASCD due to coronary spasm, three patients died during the follow-up periods. One patient died due to PEA despite the continuous electrical therapies delivered by the ICD, second patient died due to intractable ventricular fibrillation and third patient died due to electromechanical dissociation and severe reduced left ventricular contraction despite appropriate ICD therapy. All 44 except three patients with appropriate ICD shocks were rescued from second ventricular fibrillation or tachycardia. Successful recovery from second ASCD was 93.2\% (41/44) in patients with ASCD due to coronary artery spasm after the implantation of ICD, while ICD could not rescue in two PEA patients and one refractory ventricular fibrillation. Coronary artery spasm patients with ASCD may be good candidates for implantation of subcutaneous ICD, because most of them have no need for concomitant bradycardia.
therapy, cardiac resynchronization therapy, or anti-tachycardia pacing therapy\textsuperscript{[16]}. Furthermore, cardiologist can retrieve the subcutaneous ICD devise, when we encountered patients with ASCD due to coronary spasm and no appropriate ICD shocks under the medications for a long time\textsuperscript{[17]}.

**IX. Sequential spasm provocation tests under no medications**

Cardiologists should perform pharmacological spasm provocation tests under no medications in patients with ASCD due to possible spasm. Precise provoked spasm by a sequential spasm provocation test should be obtained to clarify the disease state. Because single spasm provocation test, such as acetylcholine (ACh) test only or just ergonovine (ER) test, has some limitations to document daily coronary spasm, we recommend the supplementary or sequential spasm provocation tests when necessary in the real world. A schema of a sequential spasm provocation test is shown in Fig. 3 according to our previous reports\textsuperscript{[18, 19]}.

**X. Sequential spasm provocation testing under the medications**

Spasm provocation tests were employed to diagnose the presence or absence of coronary artery spasm in the cardiac catheterization laboratory. However, cardiologists had no use of these tests as the decision of effectiveness of medical treatment to suppress the next fatal ventricular arrhythmias and of the requirement of ICD implantation. Medical therapy is the first line therapy in all patients with ASCD due to coronary spasm. Eschalier et al. recommended the ER tests be performed before the implantation of ICD in patients with ASCD due to possible coronary spasm\textsuperscript{[20, 21]}. When the ER test had no abnormal findings under the optimum medical therapies, they recommended individual discussion for ICD implantation; if the ER test indicated abnormal coronary responses, they recommended ICD implantation in all cases, even if the optimum therapy was being administered. If ASCD patients due to coronary spasm had abnormal pathological vasoconstrictions by the sequential spasm provocation tests under medications, cardiologists should consult with patients for the implantation of ICD constructively. However, when ASCD patients due to coronary artery spasm had no abnormal responses by the sequential spasm provocation tests under sufficient medications, physicians may be able to medicate these patients without ICD. It may be better to perform a sequential spasm provocation test under sufficient medications at least one or three months’ later as shown in Fig. 4. They should perform these testing in the cardiac catheterization laboratory with sufficient drug load.

\begin{figure}
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\includegraphics[width=\textwidth]{fig3}
\caption{Schema of a sequential spasm provocation test. ACh: acetylcholine, ER: ergonovine, LCA: left coronary artery, RCA: right coronary artery}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{fig4}
\caption{Clinical schedule of sequential spasm provocation tests in patients with ASCD due to spasm. ASCD: aborted sudden cardiac death}
\end{figure}
preparations for complications.

XI. Mechanical therapy for ASCD patients due to pure coronary artery spasm without Brugada syndrome or early repolarization syndrome

We should perform the electrophysiological or arrhythmic study in ASCD patients with pure VSA as well as the sequential spasm provocation tests. If the electrophysiological or arrhythmic study showed the abnormal pathologic responses, we should implant the ICD in these patients. Some VSA combined with Brugada syndrome or early repolarization syndrome. These patients’ clinical outcome was unfavorable compared with pure VSA. In this review, we mainly mentioned about ASCD patients with pure VSA. We reported the clinical benefit of sequential spasm provocation tests in patients with refractory VSA under the sufficient medical therapies. If a provoked pathological vasoconstriction is not noted on a sequential spasm provocation test under the abundant medical therapy in patients with ASCD due to coronary spasm, cardiologists and patients are free to select a course of mechanical therapy without ICD implantation. However, if a single spasm provocation test, such as an ACh or ER test alone, showed the abnormal coronary responses under abundant medical therapies, it may be better to implant ICD. The indications of mechanical treatment in patients with ASCD due to pure coronary artery spasm have not been established. As one of option, we indicated the mechanical strategy schema in patients with ASCD due to pure coronary artery spasm by the sequential spasm provocation tests under the medical therapy in Fig. 1 and 2. If we performed the prospective sequential spasm provocation tests under sufficient medications in patients with ASCD due to coronary spasm in the future, we may be able to classify the patients who are necessary to implant the ICD to suppress the next fatal arrhythmias due to coronary spasm. However, cardiologists should make comprehensive judgement for mechanical therapy in consideration of not only the coronary response of the sequential spasm provocation tests under medications but also medication adherence for each case. Further studies are also necessary to investigate the requirement of the mechanical therapy, such as ICD or advanced next generation pacemaker, in patients with ASCD due to pure coronary spasm. And further follow-up study with the clinical usefulness of the sequential spasm provocation tests under optimal medications about ASCD patients due to coronary spasm is needed.

XII. Conclusions

In patients with ASCD due to coronary artery spasm, cardiologists should pay more attention to treat with sufficient medications as well as the implantation of ICD. If cardiologists performed the sequential spasm provocation tests under the sufficient medications in ASCD patients due to pure coronary spasm as one of option for the ICD implantation, we may classify these ASCD patients for the requirement of ICD implantation to suppress the next life-threatening ventricular arrhythmias in the future.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

References


